FISKE FUND PRIZE ESSAY.

ART. XII.—*On "The Morbid Effects of the Retention in the Blood of the Elements of the Urinary Secretion."* By WILLIAM W. MORLAND, M. D. (With two woodcuts.) The Dissertation to which the Fiske Fund Prize was awarded, July 11, 1860.[1] (Published by request of the Rhode Island Medical Society.)

No organs in the human body play a more important part in the economy of life and health than the kidneys—their office is *the depuration of the blood.* In however slight a degree their function is interfered with, some untoward effects are produced. These may often be barely noticed, and easily recovered from; in many instances, however, although disregarded at first, they are sure of their ground, hard to be dislodged, and too frequently insidious and widely and surely destructive. The more open and overwhelming attacks of disease, which, by rapidly disabling the kidneys, and extensively injuring their tissue, at once and distinctly tell upon the constitution, reveal in plain characters the close connection between the vital torrent and its purifying agents.

The subject, as proposed by the Trustees of the Fiske Fund, necessitates, *first,* the enumeration of "the elements of the urinary secretion;" and *secondly,* the recital of the effects produced by the undue "retention" of each of them in the blood.

By the expression "elements of the urinary secretion," as here used, we understand its constituents in a state of health. These constituents, by a vital law, are to be eliminated from the blood; and their retention therein, beyond a certain time, will certainly cause "morbid effects."

The following enumeration of the urinary elements is taken from one of the latest and most reliable authorities.[2] The analysis is made up from an average of the composition of all the urine passed in twenty-four hours. *Average quantity* from twenty-four hours, 1400 to 1600 cubic centimetres;

[1] The Trustees of the Fiske Fund, at the annual meeting of the Rhode Island Medical Society, held in Newport, July 11, 1860, announced that the premium of one hundred dollars offered by them on the following subject: "The morbid effects of retention in the blood of the elements of the urinary secretion," had been awarded to the author of the dissertation bearing the motto—

"*Prius cognoscere, dein sanare.*"

And upon breaking the seal of the accompanying packet, they learned that the successful competitor was Wm. W. Morland, M. D., of Boston, Mass.

JAMES H. ELDRIDGE, M. D., East Greenwich,
CHARLES W. PARSONS, M. D., Providence,
HENRY E. TURNER, M. D., Newport,
Trustees.

S. AUG. ARNOLD, M. D., Providence, *Secretary of the Fiske Fund.*

[2] J. L. W. Thudichum, M. D., Lecturer on Chemistry at the Grosvenor Place School of Medicine, &c. "A Treatise on the Pathology of the Urine, including a Complete Guide to its Analysis." London, 1858.

49 to 56 fluidounces. *Average specific gravity*, 1.020. *Mean amount of solids*, 55 to 56 grammes (a gramme is 15.4440 grains, English).

Constituents.

Water	1345 to 1534 grammes.		
Urea	30 to 40	"	= 463 to 617 grs.
Uric Acid	0.5	"	= 7.5 "
Creatine	0.3	"	= 4.5 "
Creatinine	0.45		7.0 "
Sarkine, Uræmatine, Uroxanthine	Undetermined.		
Hippuric Acid	0.5	grammes.	7.5
Chlorine	6 to 8	"	= 92 to 123 "
(or Chloride of Sodium	10 to 13	"	= 154 to 200 ")
Sulphuric Acid	1.5 to 2.5	"	= 23 to 38 "
Phosphoric Acid	3.66	"	= 56 "
Potash and Soda, Lime and Magnesia	Undetermined.		
Earthy Phosphates	1.28	"	= 19 "
Iron	Undetermined.		
Ammonia	0.7	"	= 10 "
Trimethylamine, Carbonic Acid, Phenylic Acid, Damaluric Acid	Undetermined.		

"The minor estimates account for 48 out of 55 grammes of solids, the larger estimates for 62 out of 66 grammes of solids."—THUDICHUM, *op. cit.*

From an examination of the above table, in connection with the requisitions of the subject, it will be evident that we have only to indicate the pathological effects arising from the undue retention in the blood, of the following constituents of the urinary secretion: Water; Urea; Uric Acid; Creatine; Creatinine; Hippuric Acid; Chlorine; Chloride of Sodium; Sulphuric Acid; Phosphoric Acid; Earthy Phosphates, and Ammonia. The other ingredients of the urine, mentioned as being found in "undetermined" proportions, cannot enter into the list, in a practical consideration of the subject.

WATER.—Taking up the urinary constituents in succession, we first examine the results to be observed when that amount of *water* which should be excreted through the agency of the kidneys, is not so evacuated. This portion of our subject may be comprehensively disposed of.

A very variable amount of fluid is evacuated from the bladder at different seasons of the year, and under peculiar and differing circumstances. Thus, in cold weather, the amount of urine is greater, because the cutaneous transpiration is less. Again, when large amounts of liquids are ingested, somewhat corresponding quantities are excreted by the kidneys. The action of abnormally produced sugar occasions diabetes; certain medicines induce or augment, whilst others restrict, or nearly suspend, the urinary flow. Organic disease, or accidental obstruction, may cause almost complete cessation of urination; and entire *anuria*, although rare, occurs, from well-known causes.

Whatever, therefore, essentially diminishes, or actually suspends, for a longer or shorter time, the urinary evacuation, causes the retention in the blood of *all* the constituents of the urine, or of a goodly proportion of them. The deleterious effects consequent upon such a retention, will be

referable, in the main, to the presence of the solid constituents of the urine, rather than to that of an unusual supply of the watery vehicle. A certain amount—a redundance, even—of water, is absolutely necessary in the circulation, in order to eliminate, wash out, and bear on, as through a sewer, the effete, nitrogenous products, foreign to life, and incompatible with the integrity of the blood. And, besides this necessity for a surplus amount of water, it is rare that enough more than a normal amount is retained in the blood, to be of essential consequence, compared with the effects arising from the presence of the solids of the urinary secretion, prevented from issue by the same cause or causes which retain the watery portion. It is true, however, that "when urea is retained, water is also mostly retained in part, and, by its effusion into the cavities and cellular tissue, causes dropsical disease." (*Thudichum*, op. cit., p. 75.) But the action of the causes just alluded to is rarely or never sufficiently long maintained to be efficient in producing a deteriorated condition of the blood, *referable to excess of water alone*, the kidneys being healthy. Other morbid influences, arising from the presence of the solids of the urinary secretion, and the persistent action of the retaining cause upon the organs themselves, would produce far more rapid and appreciable effects upon the system at large, and upon the blood, than a simple increase of water, only, could do. It is acknowledged, however, that scanty urine—diminished both as to solid and fluid constituents—is indicative of a greater or less degree of anæmia. On the other hand, symptoms of hydruria may be favourable in certain diseased conditions—as where hydræmia and dropsy exist—and its actual establishment, either naturally or by artificial diuresis, may carry off the misplaced water, and restore the balance of the circulation. The profuse flow of watery urine in hysteria is often critical—at all events, *per se*, it indicates no blood-disease. Co-existent anæmia, in such cases, doubtless depends on some other cause than retention of the water of the urine in the blood, or its mere redundance. Often, also, where the quantity of urine excreted is very small, the skin, the bowels, and even the lungs, act *quasi* vicariously, and thus prevent or diminish any ill effects attributable to scantiness of evacuation of the watery portion of the urine. It is well known, also, that the skin will eliminate urea, in cholera, in such quantities that it not only can be detected, but the amount appreciated. (*Thudichum*, op. cit., *et alii*.)

We may now dismiss the watery element from our subject, and proceed at once to the consideration of the undue retention of the solid constituents of the urine in the blood.

UREA.—(Symbol: $\overset{+}{U}$.—Formula: $C_2H_4N_2O_2$.)[1]

This substance, "the principal product of the metamorphosis in the body of nitrogenized food," and always a constituent of healthy urine, is considered a blood-poison when retained in the circulation. Some observers

[1] Bird, Thudichum, *et al.*

Chemical Composition of Urea.

	THUDICHUM.	G. BIRD.
2C	20.000	$C_2N_2H_4O_2 = 60$.
4H	6.666	
2N	46.667	
2O	26.667	
	100.000	

believe its action to be direct, others that it is indirect—or exerted through the agency of a product of its decomposition. It forms the most considerable portion of the solids of the urinary secretion, and is purely excrementitious matter, the elimination of which by the kidneys is absolutely necessary to health and life. It is true that, in certain exceptional instances, large quantities of it have been ascertained to be present in the blood, for a long time, without compromising life, or even exciting those cerebral symptoms usually observed under such conditions; but it is to be presumed, either that the persons were, to a great extent, insusceptible of the action of urea, or else that the peculiar fermentation supposed to give rise to uræmic poisoning, by producing a noxious substance from the urea, did not take place. It is certainly very possible that certain persons may be less impressed by the presence of urea in the blood than others; but, we repeat, such cases must be entirely exceptional. With regard to the constancy of decomposition of urea when retained in the blood, and the consequent formation of another and a toxic substance, we have, as yet, too few facts to enable us to determine. If ever proved to be the rule, however, the intervention of certain unknown agencies might, in isolated instances, prevent its execution; and thus account for an apparent, or at least a temporary, immunity from morbid consequences.

After extirpation of the kidneys in animals, and in Bright's disease and some other affections, urea is found pervading many of the fluids of the body—as, the dropsical effusion, the blood, the perspiratory secretion, the vitreous and aqueous humours, and the liquor amnii.[1] Dr. Thudichum, who refers to its detection in the latter fluid by Wöhler, considers its presence there as exceptional; and is inclined, moreover, to throw doubt upon many of the reported instances of its occurrence in other fluids—the reports being in several instances merely assertions by the authors, and not ratified by proof, or else erroneously or partially quoted. Urea has also been declared to have appeared in the milk,[2] in the serum from blisters, and in the alvine evacuations of patients with diseased kidneys.[3] Dr. Rees states that he has "found most unequivocal evidence of its presence in peritoneal, pericardial, and pleural effusions, and also in the fluid of the arachnoid."[4]

With regard to the question, already alluded to, whether urea retained in the blood is directly or indirectly deleterious—that is, whether it acts *per se* as a poison, or becomes such by a process of decomposition, in which case the carbonate of ammonia is believed to be the injurious agent—there has, of late, been much discussion. The latter view has its zealous advocates, and their theory seems to be somewhat gaining ground. As we have already intimated, there are significant facts adverse to the conclusion that urea alone, as such, is a blood-poison. Dr. Bright remarked that urea may long exist in the blood, in renal disease, and yet no cerebral symptoms arise until the very last of life. He mentions one case which lasted from four to five years. Dr. Rees gives even stronger testimony. He found, in a patient who had no uræmic symptoms whatever, but who retained his cerebral functions to the last moment of his life, the blood more highly charged with urea than he had ever known it in Bright's disease. Dr. Johnson, of London, in his

[1] The presence of urea in the fluids of the body was first announced by Dr. Christison in the Edinburgh Medical and Surgical Journal, October, 1829.

[2] Rees, Diseases of the Kidney, London, 1850, p. 46. Albuminuria existed in the patient.

[3] Dr. Golding Bird—after the action of elaterium.—*Urinary Deposits.*

[4] Loc. cit.

justly celebrated work on diseases of the kidneys, affirms that no actual proof exists that urea is the poisonous agent, or, at least, that it is the only one. If admitted to have a poisonous influence, he holds that some peculiar, unknown condition of the blood must exist, to favour its toxic action. Frerichs is the author of the theory that carbonate of ammonia, resulting from a decomposition which the urea undergoes in the blood, is the poisonous agent. Its presence in the blood he indubitably ascertained, and by injecting it into the bloodvessels of dogs, he produced convulsions. Dr. Hammond, U. S. A., has made some interesting experiments, with the intention of testing this matter. He injected urea, vesical mucus, sulphate of soda, nitrate of potash, and carbonate of ammonia into the blood of dogs; in some instances removing the kidneys previous to injecting the substances. He did not detect ammonia in the breath of any of the animals operated on with *urea* by injection. He inclines to pronounce its presence in Frerichs's cases purely accidental. The animals from whom the kidneys were removed all died, after strong convulsions; and Dr. H. infers an analogy between animals deprived of the kidneys and patients affected with Bright's disease. Such analogy, it is true, may be predicated; but many attendant circumstances attaching to the cases of persons with diseased kidneys do not, of course, affect animals *without* kidneys, and consequently the analogy is not perfect, and hardly as safe to reason from as even the proverbially insecure foundation derived from analogical reasoning generally. Dr. Hammond does not find that urea or carbonate of ammonia, injected into the bloodvessels of sound animals, causes death; if they have suffered extirpation of the kidneys, such injection proves fatal. He does not discover from his experiments that urea, introduced directly into the circulation, becomes converted into carbonate of ammonia.[1] The experiments, at all events, go to prove the deleterious agency of urea, or of the product of its decomposition, when not promptly excreted from the blood, whether it be due, as in the case of the animals experimented upon, to loss of the kidneys, or, as in certain conditions in the human subject, to its retention in the blood by diseased, perverted, or obstructed action of those organs. While the question as to the exact material acting poisonously is still in abeyance, the *facts* relative to urea retained in the blood as productive of various "morbid effects," are indisputable, and as such we shall now proceed to examine them.[2]

GENERAL PHENOMENA REFERABLE TO THE PRESENCE OF UREA IN THE BLOOD.—From the fact that Bright's disease is the affection in which urea is most frequently retained in the blood, it will be all the more necessary not to refer any of its concomitant phases to the action of urea solely; although it is very plausible, and some of the best medical observers of the present day are beginning to teach, that many of the so-called *sequelæ* of Bright's disease may legitimately be referred to the presence of urea in the circulation. Thus, Dr. Watson remarks the extreme readiness of various organs of the body to become inflamed during an attack of Bright's disease. Especially is this found to be true, as all observers will testify, in reference to the serous and mucous membranes. Dr. Watson himself calls attention to this fact, and cites Drs. Bright, Christison, and Gregory to the same effect. He mentions, also, that M. Solon does not, in his volume on albuminuria, consider this tendency especially prominent in France.

[1] North American Medico-Chirurgical Review, March, 1858.
[2] See Appendix, note A.

Bronchial, pleural, pericardial, peritoneal, gastric, and intestinal inflammation are well-known and common *sequelæ* of Bright's disease, and occur, as to frequency, very nearly in the order above named. Now, it is very plausible to suppose that the abnormal condition of the blood, caused by the presence of urea, may be productive of many of these manifestations. Dr. Watson, while suggesting this, speaks particularly of disorder of the stomach and bowels, which so often follows or is concomitant of Bright's disease, and considers it may be explained by the action of "the poisonous material retained in the blood, and seeking a vent through supplementary channels of excretion."[1] He then refers, as corroborative proof, to the *post-mortem* appearances observed in these cases; "most commonly evident traces of disease are met with in various organs" besides the kidneys. This distinguished observer adds, that these manifestations "prevail with irregular frequency in different places. They are probably determined, in some measure, by local and peculiar agencies. Thus, vomiting and diarrhœa have been more familiar to the Edinburgh observers, than in London to Dr. Bright, or in Paris to M. Solon; while the headaches and coma so often witnessed by the British physicians have been comparatively uncommon in France."[2]

Although, in abnormal retention of urea in the blood, the vital tissues and fluids are all more or less affected, and, by a concomitant disturbance of the watery as well as of the solid portions, dropsical effusion may arise, yet the spinal cord and brain are the organs chiefly affected whenever urea becomes a blood-poison; and we have seen that the instances where it is not thus morbidly efficient, when retained in the blood, are exceptional. Generally speaking, when the amount of urea thus traversing the system is considerable, its effects are decided and rapidly disastrous. The affection is, properly, a cachectic condition; in other words, the system is, throughout, evidently depressed by a poison.[3] Were it not, moreover, that the disease of the cerebro-spinal system, consequent on uræmia, is usually so severe, persistent, and fatal, the blood would become very seriously altered in its constituent parts, and finally devitalized, by the retention of urea; and, in addition, the whole play of the vascular system would be disturbed. The large quantities of albumen often eliminated during the retention of unusual amounts of urea in the blood cannot be said to be referable to the presence of urea alone. Albuminuria and uræmia may coexist, but the union is not a necessary one; neither is directly causative of the other. This fact we find pertinently referred to by Prof. G. S. Bedford, in his short but instructive chapter on uræmia.[4]

If we were to investigate thoroughly the disturbed chemistry and proportions of the blood which might properly be imputed to retention therein of the solid constituents of the urine, the limits of an essay, such as the re-

[1] M. Claude Bernard (Leçons sur les Propriétés Physiologiques et les Alterations Pathologiques des Liquides de l'Organisme. Paris: J. B. Baillière, 1859) remarks that in renal disease, when the urine is suppressed, intestinal disorder supervenes. The bowels have taken up, so far as they can, the elimination of urea. The rule is, that there is an elective affinity manifested by certain glands in the elimination of certain products from the blood. When anything interferes with their action, others fulfil their office to the best of their ability.

[2] Lectures on the Principles and Practice of Physic, fourth edition, London, 1857, vol. ii. p. 682.

[3] Notwithstanding that many of the cerebro-spinal phenomena observed are those of irritation or excitation.

[4] Clinical Lectures on the Diseases of Women and Children.

quirements of the question now proposed seem to demand, would be soon attained, and, by the addition of the practical details, largely exceeded. We have interpreted the terms of the subject as indicating a desire for an exposition of the phenomena of disease believed to be legitimately referable to the abnormal retention of the solid urinary constituents; and whilst endeavouring to present these, most of the results of the disturbed proportions and composition of the blood will, in fact, be made evident. And, in concluding these general remarks, it is well to say that accomplished observers, some years since, have been inclined to ascribe many manifestations of disease of slight intensity, and previously obscure and very imperfectly understood, to the presence of abnormal quantities of urea in the blood.[1]

I. CEREBRO-SPINAL PHENOMENA ATTRIBUTABLE TO UREA RETAINED IN THE BLOOD.—(A.) A drowsy condition is often the first distinctly declared manifestation of toxæmia by the presence of urea or of the product of its decomposition in the blood. There are sometimes premonitory symptoms of less clear significance, but not always. Some writers, however, class them among the recognized *prodromata*.[2] This drowsy state ordinarily deepens into stupor and true coma, if it be impossible to relieve the blood of the offending element. The re-establishment of free diuresis, or a tendency to recovery from renal disease, may effect so desirable a result; but, unfortunately, the tide too frequently sets in the opposite direction. Coma may prove the final phase of the affection, and be simple or unaccompanied by disordered motility; or it may be combined with convulsions, and life may be terminated even more rapidly than if the complication had not existed.

(B.) Convulsions of an epileptic form may be the sole manifestation; there being no sopor, and consciousness being intact. The state is, in every respect, fully as unpromising as either of the two just indicated.

Among the first symptoms of uræmia may be mentioned—œdema in various parts of the body;[3] lowness of spirits, amounting at times to me-

[1] Urea is always present in healthy blood, but in very small proportion. It may sometimes even not be readily recognized. Morbid effects, consequently, depend upon its presence in large quantities, and upon its *accumulation*, in the blood. The abnormal increase, therefore, even if small, will exert an influence. For valuable chemical and physiological information on this point, see the works of Simon, Thudichum, and Carpenter.

[2] These will be specified hereafter; they are of a character less arrestive of attention than the others; we will only mention—confusion of ideas, failure of memory, unusual sluggishness, general *malaise*.

[3] This peculiar feature of the affection deserves especial notice. Its seats are chiefly the upper part of the body, the face, and the extremities—both upper and lower. The *labia majora* not infrequently exhibit it. Change of the patient's position often causes its disappearance, temporarily; and it frequently becomes less marked, or even vanishes, towards the end of pregnancy, even while the albumen of the urine and the structural disease of the kidneys is increasing. (Braun.) "The skin of the non-œdematous parts of the body appears very dry, and as white as chalk (chlorotic, hydræmic, leukæmic), and has a low temperature. Only those œdemata of pregnant women which exist contemporaneously with albumen, fibrin cylinders, and fatty degenerated scales of Bellini's epithelium in the urine, have a connection with uræmic eclampsia. The œdema of the lower extremities, ascites, and hydramnios, which are not complicated with albuminous urine containing fibrin cylinders, are not followed by uræmic eclampsia in pregnancy and labour. The affection of the kidneys with disease cannot certainly be inferred from the appearance of dropsy, as distinct causes may, at the same time, or one after the other, produce dropsies." (Braun, *Uræmic Eclampsia;* Duncan, p. 17.)

lancholia; restlessness; dizziness; headache; fretfulness; partial anæsthesia and delirium. Nausea, retching, vomiting, and rigors, are likewise noticed. There are often, also, impaired vision, amblyopia, muscæ volitantes, and amaurosis. These latter symptoms, as indeed all the others, are especially mentioned by Dr. Braun, of Vienna, in his late work on Midwifery; a chapter from which, devoted to Uræmic Eclampsia, has been ably translated by Dr. Duncan, of Edinburgh, and has furnished us with a great deal of new and valuable information. While Dr. Braun's views with regard to the subject of uræmic eclampsia will, doubtless, not be at present received as a whole by the profession, and are, indeed, questioned in many points by his translator, yet his extensive research, accurate observation, admirable description, and ingenious reasoning, render the chapter to which we refer at once entertaining, instructive, and full of practical suggestions. We acknowledge our great indebtedness to the author and his translator.

When stupor and coma finally supervene, a greater or less degree of apoplectic stertor accompanies the respiration. It is uniformly noticed that this stertor has a peculiarly *high tone*—a sort of shrillness, distinguishing it from ordinary apoplectic snoring. Reference was first made to this fact by Addison (*Guy's Hospital Reports*, 1839, No. VI.), and is repeated by Reynolds (*Diagnosis of Diseases of the Brain*, &c., London, 1855) and by Rees (*On Diseases of the Kidney*, 1850).[1]

The action of the poisonous agent in uræmia is believed by the best authorities (Tyler Smith, Braun, Reynolds, Churchill, *et al.*) to be first directed to the spinal marrow; and hence the sensitive impressions which make themselves morbidly apparent, as dizziness, headache, and subsequently convulsive movements. We are not to inquire into the *modus operandi* or etiology of uræmia, or of the other diseased conditions supervening in the human subject, upon retention of the elements of the urinary secretion in the blood; but—as we understand the question—to state the "morbid effects" only; consequently, we shall not occupy time and space by setting forth the received views and theories as to the direct or indirect modes of transmission of the deleterious influences, but will endeavour to state succinctly the disordered vital phenomena observed, and the pathological appearances, if any, which are noted *post mortem*.

[1] Dr. Reynolds, commenting upon this characteristic, writes thus: "The stertor exhibits a peculiarity first noticed by Dr. Addison. It is not of low, guttural tone, but of much higher pitch, and appears to be caused by the mouth rather than the throat, either by some position of the tongue against the roof of the mouth or teeth, or by some movement of the arches of the palate, not like that causing ordinary stertor, from which (although its mechanism is obscure) it presents the most obvious difference. (In several obscure cases—*i. e.*, obscure from the fact of the patient's not having come under notice until cerebral symptoms had appeared and consciousness was so far lost that no commemorative history could be obtained, and in which no œdema of the ankles was perceptible—this peculiarity of the respiratory stertor has at once awakened my suspicions; has led to an examination of the urine and the breath, and to the discovery in the former of albumen and fibrinous casts, and in the latter of an undue quantity of ammonia.") (*Op. cit.*, p. 110.) The latter fact is significant, in view of the doctrine of Frerichs as to the agent which proves poisonous in uræmia; and the experiments and observations of many others go far to confirm the opinion.

Dr. Reynolds adds: "The peculiar muscular condition causing this stertor, I am disposed to consider as the result of spasm rather than paralysis, and the spasmodic contraction may be either of sensori-motor, simply reflex, or tonic origin, forming only one of many phenomena which indicate excessive or perverted conditions of those groups of motor action. This hypothesis is, of course, as unimportant as the fact of the difference is valuable."

Uræmic symptoms may, of course, arise in both sexes from renal disease, or from mechanical obstruction to the excretion of the urine, as in hydronephrosis, retroversion of the uterus, urethral stricture, and closure of the ureters; which latter, if dependent on an unrelievable cause, must soon prove fatal. The occurrence of what has been termed "uræmic eclampsia" has been witnessed in non-pregnant females, and in males, and so cannot be considered as invariably belonging to the parturient state when urinæmia exists. The portion of Dr. Braun's work already cited, is devoted to the exposition of his belief that the convulsions observed during pregnancy are almost exclusively dependent on urinæmia.

After the appearance of the premonitory and of the earlier symptoms of uræmia, the progress of the mischief will, of course, be variable in different patients, and also according to the amount and *cause* of the retention of urea. Thus, it would seem natural that a large amount of urea being somewhat *suddenly* thrown into the circulation, and kept there by the continuance of the cause, should prove rapidly disastrous, and be accompanied with marked and violent phenomena. When gradually introduced, as in the slower advances of renal disease, or by the action of a progressive obstruction, the system may become somewhat accustomed to the presence of the deleterious agent. May not this be, in some degree, the explanation of the innocuousness of those very considerable amounts of urea the presence of which in the blood, and for a prolonged period, was ascertained by such accurate observers as Bright, Christison, Frerichs, and Rees; in conjunction, as we have previously intimated, with a possible greater power of resistance to the urea-poison in some constitutions than in others?[1] If this explanation be not in any degree admitted, the only alternative seems to be to accept the theory of Frerichs, that carbonate of ammonia is the toxic agent. In support of this view, we have the experiments upon animals, already referred to, in part, where extirpation of the kidneys was practised—as by Prevost and Dumas, Segalas, Tiedemann, Gmelin, Mitscherlich, Claude Bernard, Barreswil, Stannius, and Frerichs, all cited by Dr. Bedford to prove this point (*op. cit.*); and the test by injection tried by Bichat, Courten, Gaspard, Vauquelin, Segalas, Stannius, Frerichs; both methods without inducing convulsions. (*Idem.*) Dr. Bedford also mentions the significant fact that Vauquelin and Segalas proposed to give urea as a diuretic, so little did they consider it a poison! It is, under the present aspect of the subject, as well not to try the experiment.

Orfila—to come to direct experiments—caused fatal convulsions in an animal by the administration of carbonate of ammonia; and Bernard and Barreswil found carbonate of ammonia in the stomach and intestines of animals after extirpation of the kidneys.

Dr. Rees's idea that a peculiar "tenuity" of the blood may be requisite, in order to have full toxæmic action, when urea is retained, is certainly plausible: for we may at least suppose that the poisonous matter will be more readily and abundantly distributed through the circulating medium, and will consequently more thoroughly pervade and act upon the system.[2] And

[1] Frerichs states that the presence of the as yet unknown *ferment* in the blood is necessary, in order to the production of toxæmic symptoms by generation of the carbonate of ammonia. He thus explains the toleration of so much urea in certain cases.

[2] Dr. Todd ("Lumleian Lectures on Delirium and Coma," *Med. Gaz.*, 1850) also favours this idea. He believes the poisonous action of urea is facilitated by impoverished blood.

here we cannot refrain from adducing the exceedingly acute and ingenious remarks made upon this point by Prof. Simpson, of Edinburgh (*Obstetric Works*, vol. i. p. 371, American edition), in the article containing his statements in reference to puerperal convulsions, which latter, as we have already mentioned, recent observers have distinctly referred, in a large majority of cases, to toxæmia by the retention of urea, or of the product of its decomposition, in the circulation. In this particular connection, however, the patients were children—so that here we have remarkable instances of direct uræmic poisoning in connection with albuminuria—convulsions being the prominent symptom. The account of the first case we transcribe entire, together with a foot-note of much interest.

"A few weeks ago, I saw an instance in which convulsions in a child after birth were connected with the presence of albuminuria in its urine; or connected, as it should be, perhaps, more correctly stated, with that condition of the blood-poisoning or uræmia which is the result of albuminuria—whether that condition consists in a morbid accumulation of urea, or is produced, as Frerichs supposes, by the presence of carbonate of ammonia in the blood, produced by decomposition of the urea, or is, as is more probable, the effect of some other morbific agent in the circulating system, capable, like strychnia, of increasing the centric irritability or polarity of the spinal system to such an excessive degree that, under this super-excitability, comparatively slight eccentric causes of irritation in the stomach, intestines, uterus, bladder, &c. &c., readily induce convulsive attacks of a general form, like those of puerperal eclampsia." (*Loc. cit.*)

In the foot-note appended to the above passage, and in reference particularly to the theory of Frerichs, Professor Simpson makes the following important and interesting suggestions:—

"If the blood-poison, which in albuminuria produces convulsions and coma, be, as Frerichs believes, carbonate of ammonia, resulting from decomposition of urea, can we account for the power of chloroform in restraining and arresting, as it does, puerperal convulsions, upon the ground of its preventing this decomposition? The inhalation of chloroform produces, as various chemists have shown, a temporary diabetes; sugar appears in the urine, and hence, probably, also in the blood. The addition of a little sugar to urine *out* of the body, prevents, for a time, the common decomposition of its urea into carbonate of ammonia."

After mentioning the death of another child from convulsions supervening on the third day after birth—the mother having had puerperal convulsions and recovered—Dr. Simpson states that Dr. Weir, of Edinburgh, and himself found the urine of the child, like that of the mother, highly albuminous. He also says he is unaware of any reported observation of the coexistence of albuminuria and infantile convulsions; and then hints at the possibility that the albuminuria may be common as a pathological condition in certain forms of the convulsions of infants—as in trismus nascentium. Other infantile diseases, he thinks, may be powerfully influenced by albuminuria—as, for instance, sclerema, the "endurcissement ou l'œdeme du tissu cellulaire" of French writers. Dr. Simpson had only seen two cases of this in Edinburgh, but was led, at the time of observing them, to believe and "to suggest that the skin-bound disease itself, or at least some forms of sclerema, may be a variety or effect of Bright's disease in early infancy; the effusion into the cellular tissue, which constitutes the marked feature of the affection, being so far analogous to the anasarca occurring with albuminous nephritis."

In reference to the use of chloroform, and the explanation which Dr. Simpson attaches to its mode of action in overcoming puerperal or uræmic

convulsions, may we not ask whether the subduing power of the anæsthetic agent, acting as it does upon the cerebro-spinal system, directly, is not sufficient, of itself, to explain the control of the convulsive manifestations, without a resort to the exceedingly ingenious suggestion of Professor Simpson as to the chemical explanation of the result?

We may here remark that, in one case, Dr. Duncan, of Edinburgh, found that the inhalation of chloroform aggravated the stertor and lividity of countenance observed in a case of puerperal convulsions ("uræmic eclampsia" of Braun and others). We observe that the chloroform was administered in "small quantity"—perhaps Dr. Simpson might say the amount was not sufficiently large.

In a valuable note to a portion of the chapter of Dr. Braun's work which he has translated, Dr. Duncan has virtually enunciated the same opinions as Dr. Simpson's, previously cited—both in reference to increase of the nervous irritability acting on various organs, and to the analogy of action to be predicated from the experiments instituted by zealous students of these phenomena upon animals. We append his comprehensive and apposite remarks:—

"In uræmia, the most important point is the circulation of a morbid fluid in the nervous system, which probably does not act as a direct excitant of the convulsive motions, so much as it increases the irritability of the nerves, and the consequent liability to convulsions from exciting causes, which, under other circumstances, would produce no noticeable disturbance. Ingenious experiments have, as is well known, been performed on frogs, which seem to demonstrate an analogous condition to exist under poisoning by strychnia, at least when moderate quantities of the poison are administered." (*Loc. cit.*, pp. 59, 60.)

When the peculiar conditions to which the retention of urea in the blood is due, can be relieved and removed, we may witness rallying, and final recovery, even from very unpromising states. Persistence of the cause, however, by maintaining the presence and increasing the amount of the poison, soon induces the gravest accidents, and must terminate fatally, sooner or later, according to the violence of the attack, and the power of resistance manifested by the patient. It will serve at once the purpose of illustrating this fact, and of furnishing a synoptical view of the effects of urinæmia, to recapitulate and condense the phenomena observed under the established morbid conditions of the affection.

1. *External Appearance of the Patient.* (*Early Stage.*)—Aspect, that of general feebleness; and, if the depraved state of the blood follow scarlatina or Bright's disease, a more marked pallor, than when other causes are operative in retaining the urea in the blood—together with a puffiness about the cheeks and eyelids. Generally, sallowness, and anæmic hue, but sometimes blueness and congested appearance of the skin. More or less œdema of the extremities. Listless, confused, semi-idiotic manner.

(*Second Stage*).—Appearance that of a person apoplectically somnolent; degree, partial or complete; *modification*, by clonic contractions of the muscles.

(*Third Stage*).—Appearance that of one suffering from epileptic convulsions.

Either of the last two stages may be present singly, the other not occurring; or they may be combined and alternate.

2. *Disturbed Sensorial Manifestations. Early Stage.* ("Premonitory" of certain writers.)—Impaired vision; transient, partial and incomplete

amaurosis (Reynolds, *op. cit.*); muscæ volitantes; tinnitus aurium; temporary deafness.

(*Later Stages*).—Deficient, and sometimes entire loss of sensibility; complete amaurosis; permanent deafness—the latter less common. Sensation is seriously impaired, but not very frequently wholly lost. Distinct cognizance of impressions not taken; but usual appreciation of injury to the corporeal surface, felt. (Reynolds, *et al.*)

3. *Motorial Manifestations.* (*Early Stage.*)—More or less severe *clonic* contractions of the muscles; heavy and unwilling motions; slight stertor, "even when the patient is awake." (Reynolds.)

(*Later Stages*).—Voluntary movements mainly absent; sometimes to be provoked by excitation; continuance of clonic spasms; epileptic convulsions, more or less strongly marked. Dr. Reynolds (*op. cit.*) remarks that the rigidity of the muscles observed during this period varies greatly, being sometimes excessive, "and much increased by movement of the limb."

4. *Mental Condition.* (*Early Stage*).—Listlessness; fretfulness; uneasiness; confusion of ideas, impairment of memory, or its entire loss; partial or complete, but light, delirium—noticed often during sleep, or "when falling asleep." (Reynolds, Braun, *et al.*)

(*Later Stages*).—The profound insensibility of true coma, but at first capable of dispersion—the patient can, by persistent efforts, be aroused; soon, merging of this state into that of complete and irrecoverable carus. Frerichs notices the fact that the usually mild delirium which may, but does not uniformly, attend this state, is characterized by reiteration of the same word for a long time. A maniacal state may follow the coma, when that disappears.[1]

The species of coma first referred to—whilst the patient can yet be aroused—very much resembles that arising from opium, or other narcotic poisons, acting with full force. Dr. Reynolds, referring to this fact (*op. cit.*, p. 109), says he has noticed this sort of coma in the great majority of urinæmic cases he has observed. He writes:—

"The urinous element (whatever it may be) in the blood acts probably in a somewhat similar manner [*i. e.*, to that in which narcotics act]. There is not, however, in all cases of urinæmia, the notably contracted pupil that is observed in poisoning by opium. It is interesting to observe that the sensori-motor system appears to resemble, in its pathologic conditions, the spinal (or reflective) centre, rather than the cerebral (or intellectual). It is in a state of exalted rather than depressed activity, although both sensation and motion are severed from their purely cerebral relations (*i. e.*, from forming parts of perceptible and effective volition). There are several poisons which appear to act in a directly opposite manner upon cerebrum and spine (inducing at the same time coma and convulsions), but whether they contain different elements, whose action is thus separated, as Dr. Walshe once suggested, in a clinical lecture, the poison of urinæmia might be, I leave for future researches to decide."

5. *Special Functional and Organic Manifestations.*—In addition to the external appearances of the patient, as exhibiting deranged function of the skin, and perverted nutrition, the stomach and bowels may become excessively irritable. The vomited and other excreted matters, we are told by several observers, exhale ammonia when tested by hydrochloric acid; and the air expired from the lungs sometimes reacts similarly under the

[1] *See foot-note, page* 34.—"Some cases of puerperal mania, accompanied by albuminuria, and where no eclamptic attacks had occurred, are alluded to by Dr. Simpson."—*Duncan* (*note to Braun*, p. 136).

same agency (Frerichs, Johnson, Litzmann, Braun, *et al.*). The *pulse*, in the comatose state somewhat slow, rises, and is, at the same time, weak and irritable, in the convulsive periods.[1]

6. *State of the Urine.*—Confirmatory of the existence of obstruction to elimination and excretion. Depuratory processes at fault. The secretion is generally *acid* in reaction to tests, and *albuminous*—although cases of urinæmia occur in which albuminuria is not an element—casts of the *tubuli uriniferi*, and also blood-corpuscles and mucus-corpuscles are discovered by the microscope; and the urea is notably diminished in the specimens of urine passed. (Frerichs, Thudichum, Rees, Braun, Reynolds.)

A febrile condition, very similar to that of genuine typhus, is observed; and especially in connection with diminished excretion of the urine, or with its entire suppression. This is denominated by Frerichs, *febris urinosa;* the French writers designate it by the same term—"fievre urineuse." There is delirium, excessive prostration, and a urinous odour pervading the excretions; and death is then imminent. Death may, in certain cases where the blood has been exceedingly impoverished and contaminated, follow epileptiform convulsions which are due simply to the deteriorated and devitalized blood. These convulsions should be distinguished from those arising from other causes. Sometimes, even in such cases, rupture of cerebral vessels may cause apoplectic coma, by effusion of blood.[2]

Should life be prolonged, and in cases where recovery is possible, and occurs, there may remain permanent injury to the general health; or special organs may be particularly acted upon. Hemiplegia, hemerolopia, amaurosis, and impaired mental vigour may be mentioned. Œdema of the lungs and serous effusion into the cavities are noticed—the cerebral ventricles, even, being invaded by an urea-bearing serum. Life is too frequently destroyed, however, to enable observers to enumerate many cases and facts bearing upon this portion of our subject.[3]

II. POST-MORTEM APPEARANCES.—It is universally conceded that very few structural changes, of consequence, and often *none whatever*, are found on necroscopic examination—after death from the mere action of uræmic poisoning—in the cerebro-spinal system. The apoplectic effusions and lacerations of the cerebral substance are only indirectly, if at all, referable to uræmia. The condition of this system is that which chiefly concerns us at this time; for we are seeking strictly for the effects, both vital and *post-mortem*, legitimately due to the toxic agent derived from the presence of urea in the blood. A full description, therefore, of what is found after death in the *kidneys*, does not seem to us pertinent to the question; for the usual and well-known renal lesions of Bright's disease are not the product, but simply the frequent cause, of the uræmic condition. We shall, therefore, endeavour to particularize the appearances presented after death by those organs which during life most strongly manifest the effects of the toxic agent, and with which it is most intimately brought into con-

[1] It may be very much accelerated, and sometimes remains frequent throughout the affection.

[2] Drs. Watson, Todd, and George Johnson, have called attention pointedly to the fact of epileptiform convulsions springing from the circulation of impoverished blood in the cerebral vessels.

[3] The *mania* which sometimes follows the comatose state in uræmic eclampsia, is generally well recovered from; but should not be confounded with that symptomatic of puerperal pyæmia.—Braun; who refers to Helm, Litzmann, "and others."

tact and relation—mentioning more succinctly such other concomitant lesions as have been observed. And in noting the necroscopic manifestations in the cerebro-spinal system, we shall speak of such cases as have manifested the gravest indications of disturbance of the nervous centres during life, and especially decided coma and convulsions.

Brain.—Anæmic appearances, and a somewhat infiltrated condition, are noted; the consistence being most frequently diminished.[1] This state occurs irrespective of any abstraction of blood during life. The membranes of the brain are not commonly congested or "hyperæmic." Dr. Braun says, also, that inter-meningeal apoplexy is even more rarely observed than hyperæmia. He adds, that Helm and Kiwisch[2] very justly consider inter-meningeal apoplexy "as a secondary phenomenon produced by impeded circulation of the blood;" while it is looked upon by Litzmann as "a result of the uræmia."

Spinal Cord.—Examinations of the cord have been but infrequently made. (Romberg knew of *none* at the time of writing his *Treatise on Nervous Diseases*, the first edition of which was published in 1840 and the second in 1851.)

Braun states that Bluff, at one examination of the spinal cavity, "found much serum in it." Dr. Duncan reminds us, in this connection, that—as Dr. Christison first showed—the serum discovered in different regions of the body often has urea in it.

Dr. Todd, speaking of the condition of the cerebrum and spinal cord, after death following renal disease accompanied by coma and convulsions, says:—

"The organic disturbance of the brain which accompanies and causes the comatose tendency, is, as I have already remarked, much less than the pulmonary affection. There we find nothing which the most zealous morbid anatomist could call inflammation; and, except the patient may have died in convulsions, we do not even find congestion—that most fertile of causes with a

[1] Romberg (*Nervous Diseases of Man*, London, 1858, Syd. Soc. Ed.) when mentioning the results of cadaveric inspections in cases of *eclampsia parturientium*—which affection, it should be borne in mind, is now referred by such high authority to uræmic intoxication—says—rather adversely to what we find recorded by others—that in the cranial cavity we generally find considerable congestion, increased density of the cerebral tissue, plastic and sanguineous extravasations between the membranes, and in the ventricles, in the latter chiefly when apoplectic symptoms, a profound sopor, stertorous breathing, &c., have been associated with the convulsive affection." (*Loc. cit.*) The points in which this account chiefly differs from that given by Dr. Braun, are the frequency of congestion, and the increase of the density of the cerebral substance, which the latter observer distinctly denies, as indeed do others. Romberg, whose whole description of the epileptiform convulsions of the parturient female is admirable, clear, and vivid, refers on the above points to Hauck (*Einiges aus dem Gebiete der praktischen Geburtshülfe;* in Casper's *Wochenschrift der gesammten Heilkunde*, 1833, vol. i. p. 133; and Velpeau, *Die Convulsionen der Schwangerschaft während und nach der Entbindung. Uebersetzt von Bluff:* Köla, 1835, p. 86). Romberg, as well as other authors, refers to the paucity of necroscopic facts connected with eclampsia puerperalis; and especially with regard to the spinal cord.* This is, even at the present day, true; but the latest observations, coming as they do from reliable sources, must be allowed the greatest weight. With regard to the appearances in the *brain*, then, a certain difference of statement exists between Romberg and other authors we have consulted. As to the *spinal cavity* and *the cord*, there are no new facts within our cognizance.

[2] Helm, Th., Med. Jahrbücher. Wein, 1839, bd. xx. s. 202; Kiwisch, Beiträge z. Geburtsk. Würzburg, 1846.—Braun, *op. cit.*, chap. VI.

* Never had been examined when Romberg wrote; but has been since.

school of pathologists which is, I hope, fast disappearing. Indeed the brain is generally anæmic," &c. * * * (*Op. cit.*)

Dr. Simpson has reported (*Obstetric Works*, vol. i. p. 732) some cases of "puerperal convulsions connected with inflammation of the kidney," wherein effusion of blood and serum into the ventricles was discovered, with destruction of the right corpus striatum and outer portion of the optic thalamus, in one patient; together with encysted and degenerated kidney (morbus Brightii), and purulent-like matter, with adherent lymph, or false membrane, in another. In a third case, purulent-looking matter could be pressed out from the renal papillæ; no effused fibrin or coagulable lymph was discovered. The microscope did not decide the "whitish turbid fluid" to be pus—only epithelial cells, in large quantity, were found. The last patient had repeated convulsions, and died comatose, but no mention is made of any cerebro-spinal lesions being observed. The effusion of blood, and the laceration of cerebral substance in the first case related by Dr. Simpson, were truly apoplectic, and not referable to the intrinsic action of urea contained in the blood; although doubtless the amount present therein must have been considerable, since Bright's disease existed.

Dr. Watson (*op. supra cit.*, vol. i. p. 493), speaking of the appearances observed after death from apoplectic coma, after having referred to such a result from the action of retained urea, uses the following language:—

"On examining the brain, we may find a large quantity of extravasated *blood* spread over its surface, or lying within its broken substance; or a considerable effusion of *serous fluid* collected within its ventricles; or we may detect *no* deviation whatever from the healthy structure and natural appearance of the organ. The congestive pressure (if, indeed, it existed) has left no prints of its action."

The following observations, from the *Manual of Pathological Anatomy*, by Drs. Jones and Sieveking, are exceedingly apposite in this connection:—

"The researches of Bright, Frerichs, and others have demonstrated the close relation of the state of the blood to cerebral disease; and science has shown, what, previously, was purely hypothetical, that the most fatal conditions may be thus induced without any palpable changes being wrought in the cerebral tissues. It does not, however, follow, that because we see no changes, none have taken place. The poison that we know to be in the blood may elude our chemical tests, and yet cause death. Then, seeing how limited our knowledge of the nervous system is, it is not to be wondered at that, although the manifestation of altered function is so great as to force the belief in its altered constitution, it is not in our power to prove the latter to the perception; but, as Dr. Watson remarks, 'whatever may be the nature of the unknown, and, perhaps, fugitive physical conditions of the nervous centres, thus capable of disturbing, or abolishing their functions, it is useful to keep in our minds a distinct and clear conception of the fact, that there must be some such physical conditions.'"

Mere uræmia, therefore—presuming the occurrence of convulsions and coma—it would appear, leaves the brain anæmic in appearance, and possibly somewhat softened (more dense, according to Romberg; refer to page 35); the more decided and destructive appearances are owing to rupture of vessels, and consequent extravasation, with its consequences, and to dilatation of the ventricles with serum.

Lungs.—These organs are constantly found in an œdematous condition, and sometimes emphysematous. Dr. Braun, recording the fact that emphysema was long since observed by Böer, says that it is now considered

"as always the secondary result of the fits"—*i. e.*, uræmic convulsions. *Op. cit.*, p. 62.

Heart.—This organ is reported to be usually "empty and flaccid." (*Braun.*) We may thence infer feebleness of circulation, and impairment of its own tonicity, and of that of the bloodvessels, by reason of the impoverished state of the blood, their natural stimulant.

Kidneys.—Generally, and according to some authors, always, the kidneys exhibit more or less extensive and advanced signs of Bright's disease. In cases where the retention of urea in the blood has been caused by some other agency—such as obstruction, etc., there would naturally be traces of congestion, and perhaps of inflammation, although not uniformly; a nearly natural state might well enough exist.

As we previously intimated, it does not seem necessary to give, in this place, an elaborate account of the changes wrought by granular and fatty degeneration of the kidney, in connection with uræmia; and for reasons already stated. Moreover, these general appearances are well known, and abundantly set forth in many treatises. Those who would see, however, an admirable and somewhat condensed account of the changes of this nature effected in the renal tissue in urinæmic cases connected with pregnancy (*eclampsia puerperalis, seu gravidarum*), should consult the chapter of Dr. Braun's work, to which we have so frequently referred. A few extracts only will be made by us, and those chiefly to call attention to certain prominent points in the renal necroscopic phenomena.

Dr. Braun bases his descriptions on the three forms of Bright's disease proposed by Frerichs.

In the first stage, that of hyperæmia and commencing exudation, the surface of the kidney is smooth, the capsule is easily removed, the plexus of veins on the surface of the kidneys is dilated, and full of dark blood." (*Loc. cit.*, p. 62.)

"The pyramidal masses [renal papillæ] are likewise hyperæmic, and their injection is striped. The mucous membrane of the pelves and infundibula is swollen, and covered with vascular arborescence; and they contain a bloody fluid. Apart from hyperæmia, the finer structures of the kidneys do not appear to be essentially injured. Hemorrhagic effusions are very frequently observed, which sometimes take their rise from the glomeruli; sometimes from the vascular plexus of the tubuli uriniferi, sometimes from the veins on the surface of the cortical substance." (p. 63.) In the first stage, the epithelial lining of the uriniferous tubes is stated not to be essentially altered; the tubes themselves are often filled with exuded blood—"fibrin-cylinders."

In the second, or exudative stage, fatty degeneration commences and progresses, the kidneys becoming large, and heavier than they are normally. The capsule of the kidney can be easily separated. The pyramidal masses are dark red. The infundibula have a dirty-red mucous surface. The glomeruli (vascular knots, Malpighian corpuscles), which may be drawn out with a curved pin, are covered with a fine granular matter, and partly with solitary or grouped fatty corpuscles, which, by the addition of acetic acid, become transparent.[1] Between the glomerulus and the capsule lies a thick stratum of firm exudation, of granular structure, and having fat droplets, and sometimes crystals of cholesterine.

[1] Wedl mentions that acetic acid rendered the fat-globules more distinct.

The contents of the epithelial cells of the tubuli uriniferi next become degenerated—they are "decomposed in aggregations of granules."

Fig. 1.

Malpighian Corpuscle, from the kidney of a patient who died of *Eclampsia Parturientium*.—(From Wedl's Pathological Histology, p. 260.) "The surface is covered, partly with a fine granular substance, partly with solitary and aggregated fat-globules, which were not further changed by acetic acid or carbonate of soda. * *"—(*Loc. cit.*)

In the third stage, that of retrogradation, atrophy of the kidney is progressively induced. The pyramids of Malpighi and Ferrein are observed to be less atrophied than the cortical layer. At their bases, granulations occur between the straight tubuli, and press the latter apart.

The width of the renal pelves is increased, and their lining mucous membrane swollen and covered with a network of "varicose vessels, of an uniform grayish-blue colour."

"In those who die of uræmic eclampsia during pregnancy, atrophy of the kidneys is less frequently observed than the first two stages of Bright's disease." (*Op. cit.*, p. 69.)

III. URÆMIA IN CONNECTION WITH PREGNANCY AND PARTURITION.—If we receive the opinions of certain modern pathologists as true, the retention of urea in the blood of the pregnant female is productive, both to herself and to the fœtus, of the most disastrous results. The views of Dr. Braun, already referred to, have been adopted by a large number of able and practical men in our profession; and, since the publication of his volume—and mainly, in Great Britain and this country, through Dr. Duncan's translation of the chapter on uræmic eclampsia—have elicited great attention, and will doubtless prove an incitement to yet more extended and close observation.

Whilst many have joined Dr. Braun in this new theory, there were at the time his work appeared, and probably still are, several distinguished names arrayed against it. These are all mentioned by the author himself, who also states the objections made by them, and gives what he considers the refutations thereof. Dr. Braun's belief, as declared in his treatise, is simply this: *that the convulsions caused by uræmic intoxication in acute Bright's disease, and puerperal eclampsia, are identical.* This proposition, as he tells us, has been energetically defended by Frerichs, Litzmann, Wieger, Oppolzer, himself, and many others; but it has been assailed by Marchal, Siebert, Depaul, Legroux, L'Huillier, Stoltz, Seyfert, Levy, in very valuable articles, and also by Scanzoni. With much anxiety these observers have tried to prove that the Brightian degenerations of the kidneys, which, it cannot

be denied, are found in the bodies of those who have died of eclampsia, are consequences merely of the convulsions—only accidental, secondary phenomena of the hyperæmia caused by the eclampsia, and of hydræmia (*plethora serosa*).

Scanzoni, whose arguments against Dr. Braun's views are summed up and given by the latter author, refers the true *eclampsia parturientium* to an "irritability of the motor system of nerves which has been induced by pregnancy, and increased by the act of delivery."

The arguments *pro* and *con* have been actively carried on; and Scanzoni's conclusions were replied to by Wieger in June, 1854, and by Litzmann in 1855. In addition, the industry and zeal of Dr. Braun have enabled him to collect a truly imposing array of facts from *post-mortem* observations made by himself and other reliable practitioners, and in the majority of which abundant evidence of Brightian renal lesions existed. In some of the cases, where hyperæmia of the kidneys was found, microscopical examination was prevented by "accidental obstacles;" but the author does not consider this "any proof of the absence of Bright's renal exudation." Dr. Braun, while setting forth these investigations, says that Wedl[1] explains the non-discovery of fatty degeneration in the kidneys in several instances of death from eclampsia, "by the fact that in many cases a dissolution of the Malpighian bodies is effected by the fluid exudation, and hence in every diffuse inflammation of the kidneys an evident fat-metamorphosis of the contents of the Malpighian capsules does not ensue."[2]

Hasse, according to Dr. Braun, has never seen eclampsia puerperalis without Bright's disease. The necroscopic and microscopic observations of Wedl, Gustav Braun, Lumpe, Hecker, Devilliers, Regnauld, Simpson, Blot, Cahen, Wieger, Litzmann, Credè, Sabatier, and Hohl have contributed to establish the theory propounded in Dr. Braun's volume.

In reference to the *etiology* of "eclampsia parturientium" ("uræmic eclampsia" of Braun), Romberg[3] only hints at the agency which Braun has distinctly announced as, in his opinion, the chief efficient cause. Thus, while the latter ably demonstrates his views as to the retention of urea, and the accompanying albuminuria, the former refers to "retention of urine owing to pressure of the gravid uterus upon the bladder;" and afterwards adds: "Future investigations must determine whether albuminuria, which often supervenes during pregnancy, may, when fully developed during the last months, possess any etiological influence." The "investigations" of Braun and others certainly seem, if not already to have determined this point, likely to lead shortly to a satisfactory settlement of the whole question.

Supposing, then, in conformity with the new doctrines thus announced, that the convulsive attacks and intervening coma observed in puerperal patients are owing to toxæmia by retained urea, let us examine the collateral results of such a condition—first, in regard to the mother; and next, as respects the fœtus. Having already detailed the general effects produced upon the system by uræmic intoxication, we may properly direct our notice, at present, to the influence exerted upon the *puerperal state*, and upon the *life* of the mother and that of the fœtus.

Referring to our previous enumeration of the results, both vital and

[1] Grundzüge der pathol. Histologie, Wien, 1854, S. 306.
[2] Loc. cit., pp. 74, 75.
[3] A Manual of the Nervous Diseases of Man; Sydenham Society's edition, London, 1853, vol. ii. p. 189.

post-mortem, which are observed after genuine uræmic convulsions, we would only add thereto that the *uterus and its appendages* are generally found healthy after eclampsia puerperalis, or, at all events, do not necessarily deviate from their usual condition after labour has terminated; unless, of course, there has been some pre-existent or concomitant disease in, or alteration of, the organs. The infrequency of metritis and peritonitis is mentioned by some observers;[1] but Churchill[2] speaks of the great tendency to abdominal inflammation after the labour is over, and quotes Denman, who first mentioned this, and Collins and others, as confirming it. Braun also refers to the danger of puerperal affections coming on after eclampsia, especially if "an epidemic of zymotic diseases prevails."

The *spleen* is said to exhibit "the large dimensions it possesses in pregnancy and childbed."[3]

We now proceed to the consideration of the special influences exercised by uræmic intoxication during the puerperal state.

1. *Influence of Uræmic Eclampsia on the Duration of Pregnancy.*—Uræmic eclampsia is generally sudden in its accession, prompt in its results; and the testimony of those who have had the most experience in regard to it, is that it either causes death rapidly, or else that it is completely and with considerable celerity recovered from. Long consequent illness and sequelæ, *from the eclamptic state merely*, are not common. The true uræmic eclampsia occurs in the majority of cases in the latter part of the period of pregnancy. It may, also, only appear at the time of the labour itself; after the child is born, and before the after-birth has been delivered; or, finally, during child-bed. When supervening within the latter half of utero-gestation, premature labour is the result—as a rule.[4]

The latter two months of pregnancy are stated to be peculiarly obnoxious to the occurrence of convulsions. (Churchill, Romberg.) The *cause* of premature labour is either excitation of uterine contractions by the power of the abnormal action going on in the nervous centres,[5] or it may be, partially at least, ascribed to the presence of a dead fœtus, whose destruction is referable to the eclamptic condition. Ramsbotham, we observe, does not think the latter occurrence a cause. Churchill queries whether it may not be such; and the supposition is at least plausible. Dr. Copland (*Dict. of Med.*) speaks of cases where "the child has been unexpectedly born during the violence of the convulsions, as if expelled by them with unwonted celerity." Again, he states that the worst forms of the attack are often attended by a firm, spasmodic constriction of the cervix uteri, preventing the expulsion of the fœtus.

2. *Influence of Uræmic Eclampsia upon the Life of the Mother.*—Although puerperal convulsions—we here use the term, let it be remembered, as synonymous with uræmic eclampsia—are comparatively a rare affection, yet they make up for the element of infrequency of occurrence, by violence of manifestation and an alarming ratio of fatality. As the liability

[1] Romberg, Velpeau, *et al.*

[2] Theory and Practice of Midwifery.

[3] Braun, op. cit., p. 62.

[4] It is well known that Bright's disease, without any other influence, will cause premature labour; Braun says this is true in about 25 per cent. of cases. Add *convulsions*, and the danger is manifestly increased.

[5] Blundell (Principles and Practice of Midwifery, Am. edit., p. 418), referring to this point, says: "Sooner or later, * * if the fit continue, parturition commences of itself, without the interference of the accoucheur; and * * a sudden emersion of the fœtus occurs." He also refers to the occurrence of delivery during convulsions, unknown to the attendants.

to an attack is greater towards the last of the period of utero-gestation, so, generally speaking, is the danger to the life, both of mother and child, at that time. Not only is this true if we merely refer the eclamptic condition to the increased sources of irritability to which the nervous system has become liable, by reason of the pregnant state and its advanced stage; but also it is easy to see that a poisoned blood is all the more likely to act with increased morbid force—especially upon fœtal life. Again, the danger from convulsions diminishes according as they approximate to the term of delivery; and we are told, by a most competent authority, that the fits diminish in force in 31 *per cent.* of the cases, cease entirely in 37 *per cent.*, and only continue of the same intensity in 32 *per cent., after the uterus is evacuated.* (Braun.)

Dr. Braun refers to 15 deaths out of 45 cases, of which he has published accounts—being exactly *one-third.* He speaks of nine cases occurring in his practice within the last three years, all of which terminated in recovery. Thirty *per cent.* of the cases, it is estimated, prove fatal. Romberg gives a higher ratio of mortality. His statement is, that above one-half of the women attacked, died within twelve, twenty-four, or thirty-six hours. Churchill finds from his statistical investigations, that the proportion of fatal cases is above one-fourth. He intimates that there has been a tendency, of late, to diminution in the mortality-rate, which, at one time, he intimates, was very much larger. It has not been thought that much, if any difference as to fatality can be ascribed to early or late supervention of the affection; at all events, lateness of attack has not been allowed more weight, in this respect, by observers, when it is a first case. Some patients have several attacks in successive pregnancies, and finally die in one. A reiteration, therefore, of the accident, must be deemed of unfavourable augury. The concomitance of coma, with apoplectic stertor, and the approximation of the fits, so that they become, as is sometimes the case, almost continuous—and especially when these conditions obtain in plethoric and strongly constituted patients—are, almost without exception, fatal elements.

Recovery from the mere eclampsia may take place; and there may be some extensive dropsical effusion, some injury to the brain or spinal cord, or a permanent and increasing œdema of the lungs, disease of the heart, etc., which will compromise life at a later period; but, as a rule, if the patient escape the eclampsia, and its *immediate* results, recovery is usually not tardy, and, moreover, is complete. The occurrence of rupture of the uterus, in itself sufficiently grave at any time, we need scarcely say, very greatly aggravates the unfavourable prognosis attaching to eclampsia. Dr. Copland remarks (*Dict. of Practical Medicine*), that puerperal convulsions "should never be considered devoid of danger, more especially when they occur after delivery, or in consequence of great exhaustion of vital power, or of uterine hemorrhage. When they are slight, are unattended by stertorous breathing, or by paralytic or apoplectic symptoms, and when parturition is so far advanced as to readily admit of its completion by art, less danger may be feared."

The balance of prognostic opinion, it will be seen, is against recovery; and Blundell speaks of *post-partum* convulsions as being the most dangerous.

3. *Influence of Eclampsia on the Life of the Fœtus.*—We have already intimated the danger arising from eclampsia parturientium to the life of the fœtus. Relatively, it is even greater than that threatening the mother.

In referring to this point, those who have had the largest experience, use such expressions as the following: "In almost all cases the child is still-born, often putrid." (Churchill, *op. cit.*) "The life of the fœtus is endangered so long as it is nourished by the uræmic blood of the mother." (Braun, *op. cit.*) "The infant almost invariably dies when the disease occurs during the last months of pregnancy; it may be saved when the eclampsia supervenes during parturition." (Romberg, *op. cit.*, p. 189.) "The infant is generally, though by no means universally, born dead, when the woman has been the subject of convulsive seizures, especially if the attack has occurred early in the labour, and continued for any length of time." (F. H. Ramsbotham, *Principles of Obstetric Medicine and Surgery.*) The latter author pointedly and happily refers to *toxæmic action* on the blood of the fœtus as the most likely cause of its death *in utero;* and mentions a case from Spence, where the child being removed alive by Cæsarean section from a mother just dead from convulsions, died itself, in convulsive paroxysms, in less than an hour. The latter statement leaves us to presume a poisoned condition of the blood. M. Ménard states, that, in the majority of cases of death by convulsions, previous to delivery, the child has been found dead; the contraction of the features and extremities denoting that it had participated in the affection of the mother. Dr. Copland, who notes this remark (*Dict. of Med.*), says that it "wants confirmation."

We thus see that the likelihood of the life of the fœtus being maintained after eclampsia has been declared in the mother, is extremely small, as might, indeed, be expected; and if the child be born alive, there is great probability that it may either not survive long, or that it will be more or less morbidly affected by the accidents occurring during its intra-uterine existence.

Hereditary transmission of eclampsia, uræmia, or Bright's disease of the kidney, to a suckling, says Dr. Braun, "has not yet been demonstrated, and only Simpson has found albuminuria in a suckling born of an eclamptic mother." Dr. Duncan, in a foot-note to the paragraph from part of which the last remark is taken, says that "if the uræmia persists in a nursing woman, urea may be present in the milk, as has been shown by several observers, and may disturb the health of the suckling."

URIC ACID.—(Symbol: $\overline{U}$. Formula: $C_5HN_2O_2+HO$.)[1]

Synonymes.—Lithic acid; Urylic acid.—PROUT, BIRD, *et al.*

This substance is the next constituent of the urine, in the order of enumeration we follow; and the effects of its retention in the blood will therefore now engage our attention.

It is recognized as a constant ingredient of healthy urine, and holds a very intimate relation to urea. (Thudichum, *op. cit.*) "It forms less than

[1] Thudichum.

Chemical Composition of Uric Acid.

	THUDICHUM.	G. BIRD.
Carbon	35.714	$C_{10},N_4,H_4,O_6,C_2,H_4,N_2,O_2+2C_4,NO_2=168$
Hydrogen	1.191	
Nitrogen	33.333	
Oxygen	19.048	
Water	10.714	
	100.000	

$\frac{1}{2000}$ part of the urine in man; but its proportion varies much in different animals." (Dr. George Johnson, *op. cit.*, p. 50.) In the blood, it is always found in union with an alkaline base; and it is not soluble in that liquid. It appears in the blood in the form of urate of soda, or of urate of ammonia. (Liebig, Simon, Thudichum.) Dr. Thudichum states that the urates are always acid salts—*i. e.*, that there is excess of uric acid—and he has advanced some ingenious reasons for denying the accuracy of Dr. Golding Bird's theory and explanation of the secretion of uric acid in the form of urates. With this chemical discussion we have no concern; the indication of the pathological states induced by retention of the acid in the blood, in the form above specified, being now our object. Before approaching the subject in detail, however, it does not seem particularly out of place to allude to a practical remark by Dr. Thudichum (*op. cit.*, p. 100) upon the deposition of the urates from the urine. Researches and observations in reference to this point, cannot fail to be of importance in the treatment of such cases. Dr. Thudichum says:—

"If the presence of a deposit of urates be taken as an indication of the saturation of urine by these salts, and if the latter be assumed ordinarily to be of the usual amount, deposits of that kind become more valuable as signs of a diminished secretion of water by the kidneys than of any other symptom. As the appearance of a deposit of urates is always accompanied by morbid sensations and objective symptoms—in the healthy by thirst at least, if by nothing more—the conclusion is simple enough. *The individual whose urine has deposited the urates does not drink water enough, and must drink more, and must drink so much that the urine, at the ordinary temperature of the air, shall remain clear.* Of course, in some cases this will be neither possible or advisable; but in most cases of acute and febrile disease it should be a plan of treatment. I have certainly seen it attended by beneficial results in many cases; I have also observed the contrary—want of water in the system—to be a source of disease."

GOUT.—Whenever, from failure to eliminate the uric acid from the blood, that substance accumulates therein, the abnormal effects of its presence do not long delay their manifestation.[1] It is well known that the ingestion of large quantities of highly-azotized food, and a rich diet generally, together with the free use of malt liquors and of acid wines—Madeira amongst others—is productive of an abnormal increase of uric acid in the system; and, consequently, luxurious livers have long constituted the majority of sufferers from gout—a malady which abundantly declares its *fons et origo*, by the tendency to abundant deposition of the *urate of soda* in different parts of the body; its seat of election being the smaller joints—as those of the toes and fingers. In the latter, the deposit is often very plentiful. We have seen not long since—and the occurrence may not be very uncommon—a patient who could write his name with his "chalk-stone" knuckles; a woful example, truly, of diverted and arrested excretion![2]

[1] Bernard recognizes the accumulation of uric acid in the blood, either by arrest of the renal function, causing its elimination to cease, or by an exaggerated production of it, as in gout. (*Liquides de l'Organisme.*)

[2] An instance of this is related by Dr. Watson (*op. cit.*), and Dr. Todd has alluded to the condition. After all, cases of this extreme nature may not be so common as we have intimated.

Dr. Garrod (*On the Treatment of Gout and Rheumatic Gout*) remarks upon this point: "Comparatively few gouty patients become the subjects of visible chalk-stones, at least to any extent, or such as to induce deformity; at the same time, I am convinced that their occurrence in a slight degree is by no means so rare as has been generally assumed. Sir C. Scudamore stated, that in 500 cases of gout he only found them 45 times, or in less than 10 per cent. From my own expe-

As has been previously mentioned, Dr. Garrod, of London, first called attention, not only to the presence of uric acid in healthy human blood, but also pointed out the fact of its abnormal amount in connection with gout. He did not, however, then wish to be distinctly understood as declaring the acid the sole *materies morbi* in that disease, as may be seen by his remarks in a "Postscript" to his highly interesting paper, communicated to the Medico-Chirurgical Society, upon the subject. This important contribution to scientific medicine was read before the Society,[1] February 8, 1848, and the postscript just alluded to bears date July 26, 1848. (Vide *Medico-Chirurgical Transactions*, vol. xxxi.)

Daily observation tends to show that the relation of cause and effect may more and more safely be predicated in regard to the presence of an excess of uric acid in the blood and the phenomena of gout. Writers upon the subject, both near the time of Dr. Garrod's first researches, and later, have varied somewhat as to the completeness with which they have expressed themselves in respect to establishing uric acid as the active agency in gout. The majority of testimony seems to be affirmative. Dr. Watson (*Principles and Practice of Medicine*, 1848) seems to have then regarded the morbid agent as recognized. We find, indeed, in the edition of Dr. Carpenter's *Physiology* published in 1846, very positive language as to the conspicuousness of uric acid in gouty affections; he says: "When it [uric acid] is imperfectly eliminated, we are assured of its accumulation in the circulating fluid, by its deposition, in combination with soda, in the neighbourhood of the joints—forming gouty concretions, or chalk-stones." He thus appeared to recognize the cause of the diseased condition as lithic acid. There are those, however, who, even at the present day, speak with less distinctness as to an excess of uric acid being the sole and sufficient *materies morbi*. Thus, Dr. Barclay (*A Manual of Medical Diagnosis*, London, 1857) writes: "The researches of recent times have gradually led to the discovery of an important element in gout—the presence of an excess of uric acid in the blood. This knowledge holds out a prospect of our arriving ultimately at more accurate diagnosis; at present, it is only in the hands of a few that such a chemical test can be relied on." The opinion is a very guarded one—decidedly non-committal; we think more influence than it implies may safely be allowed to the "element" in question.

It will, at least, not be disputed that gout is a blood-disease. Amongst many other observers who might be cited on this point, we select Dr. George Johnson, as furnishing comprehensive testimony. Referring to gout as a cause of renal disease, he says: "It would be useless to occupy the time of my readers by lengthened arguments to prove that gout is a blood-disease, since all the phenomena of the disease clearly indicate such an origin, and can be explained on no other supposition." (*Op. cit.*, p. 78.) He then alludes to the intimate connection between gout and the uric acid diathesis. Thus, then, when such a diathesis prevails, or when, by some obstructing agency, the elements of the urinary secretion are retained and accumulate

rience, I consider these numbers far below the real proportion, being confident that their existence is frequently overlooked, as they are sometimes deposited in parts of the body scarcely to be expected." Dr. Garrod thinks that gouty concretions are more frequent upon the cartilages of the ear than anywhere else; contrary to what has usually been recorded. He refers to the *Medico-Chirurgical Transactions*, vol. xxxvii., 1845, pp. 74, 75.

[1] By Dr. C. J. B. Williams, upon some of whose patients Dr. Garrod's experiments were made.

in the blood, the gouty accidents, amongst others, prevail. If uric acid be prominent, the corresponding series of symptoms seems as sure to occur, as does that following the retention of urea when *that* substance is retained, in excess, in the circulation.[1] If the uric acid, therefore, is received as the true *materies morbi* in gout, we have, at once, the following easily-deduced sequence of morbid effects:—

First, deficient depuratory action; next, accumulation of uric acid in the blood; *dyscrasia*, chemical and physiological; deposition of urate of soda in various parts; the objective phenomena of gout; the *sequelæ* of gout—amongst others, as Dr. Johnson points out, renal disease. Under the light of modern pathology, we do not think the above any too weighty a burden to lay to the charge of retention and accumulation of uric acid in the blood.

There may remain a certain quantity of uric acid in the urine, at the same time that the analysis of the blood shows an abnormal amount therein. This would indicate a large supply from some source—either from waste of the tissues, or from the excessive ingestion of highly-azotized food, to which latter cause we some time since alluded. Dr. Copland notices, in a comprehensive and satisfactory manner, the "Pathological Relations of Uric Acid and Urate of Ammonia" (*Dict. of Pract. Med.*); and M. Becquerel (*Sémiotique des Urines*) agrees with him in his views. Copland, referring to this, considers the chemical explanations offered by Liebig, in connection with certain of these pathological points, "opposed to clinical observation."[2]

Dyspepsia, with mal-assimilation of food and consequent deficient nutrition, or arrested cutaneous function and habitual costiveness, no less than obstructed excretion of the urine, may engender an excess of uric acid, and the latter may be retained in the blood. (Copland, *loc. cit.;* Chambers, *Digestion and its Derangements; et al.*) It is likewise true, conversely, that in depraved, deteriorated, and anæmiated states of the circulation, uric acid is diminished in the urine. If this ill-adjusted balance implies the throwing of an unusual quantity of the substance into the blood, the latter circumstance may have no small amount of influence, if not in causing, at least in continuing, the disorder of the blood itself and of the constitution generally. Gout occurring under such circumstances—as it is not very infrequently known to do—would be appropriately termed *atonic gout*, or what Dr. Todd (*Clinical Lectures*) terms "*asthenic gout*," in contradistinction to his "sthenic gout," where the affection occurs in robust, well-constituted, and richly-nourished individuals.[3]

In reference to the dyspeptic condition of gouty patients, often so exceedingly troublesome, Dr. Chambers (*op. cit.*, American edition, 1856, pp. 294-95) refers rather scornfully to the influence of uric acid as a noxious element. He is remarking upon the tendency of the food to become acid after ingestion, and to lie unchymified—not "passing onwards." This

[1] The blood contains, as Dr. Garrod remarks, "mere traces" of uric acid *in health*. This fact, however, in no degree invalidates the agency of the acid as *a causative element in gout*.

[2] Dr. Copland does not believe that the presence of urate of soda in the blood of gouty patients precludes "the elaboration of a portion of the uric acid and its compounds, or the modification and metamorphosis of one or more of their elements by the kidneys." (*Dict.*)

[3] These two forms of gout, we conclude, are those termed by Dr. Druitt "*high*" and "*low*" gout. (*The Surgeon's Vade Mecum*, 1859.)

state of things, so common in hereditarily gouty persons, Dr. Chambers is inclined to explain by considering its pathology "to be a slight flux of mucus, deficient gastric secretion, and yet a vigorous, sometimes even excessive appetite. Hence, they have not that check of failing desire for food which makes the meals of other invalids moderate, and eat more than their imperfect gastric juice can digest. This is a simpler, and, therefore, more probable explanation than the usual chemical talk about uric acid, &c., which might be substituted for it." It seems there is some fault in the working of the hidden *chemistry* of the body, however; and, although Dr. Chambers's explanation is doubtless very correct in reference to the influences and agencies of which he speaks, yet the overt action and manifestations of excess of uric acid, in the visible form of urate of soda concretions, sufficiently show the importance of the part it plays in the *tout ensemble* of gouty affections.

The original conclusions of Dr. Garrod, given in the admirable paper to which we have referred, were these:—

"1st. The blood in gout contains *uric acid* in the form of urate of soda, which salt can be obtained from it in a crystalline state.

"2d. The uric acid is diminished in the urine immediately before the gouty paroxysm.

"3d. In patients subject to chronic gout with tophaceous deposits, the uric acid is always present in the blood and deficient in the urine, both absolutely and relatively to the other organic matters, and the chalk-like deposits appear to depend on an action in and around the joints, &c., vicarious of the 'uric-acid-excreting' function of the kidneys.

"4th. The blood in gout sometimes yields a small portion of urea (no albumen being present in the urine)."

These conclusions were all duly sustained by analyses and experiments upon patients in University College Hospital; and the record of these demonstrations is at once satisfactory and highly interesting.

In respect to the supervention of gout in low and debilitated states of the system, to which allusion has previously been made, Dr. Garrod very clearly explains "two facts" then considered opposed to referring the pathology of gout to the humoral doctrines. We may say, *en passant*, that the humoral pathology seems the only reasonable mode of explaining the affection, and that, as may be distinctly perceived, it is coming more into favour of late, than it has been for a long time, in respect to many diseased conditions.

Dr. Garrod's remarks on the above point are:—

"Any undue *formation* of this compound (urate of soda) would favour the occurrence of the disease; and hence the connection between gout and uric-acid gravel and calculi; and hence the influence of high living, wine, porter, want of exercise, &c., in inducing it." Then, speaking of the "two facts"—viz., *hereditariness* and the supervention of gout in *low states* of the system—he says: "We can understand that the peculiarity of the kidney, with reference to the excretion of uric acid, may be transmitted; and likewise that, when the function in question is permanently injured [viz., the 'uric-acid-excreting' function], it will not require an excessive formation of the acid to cause its accumulation in the blood." (*Loc. cit.*, pp. 93, 94.)

Dr. C. J. B. Williams (*Principles of Medicine*), referring to the fact that gout had been generally admitted, by inference, to depend on the existence of an excess of uric acid in the system, chronicles Dr. Garrod's experiments and analyses, which, as we have stated, were first made on patients under Dr. W.'s care, in hospital. He says:—

"Gout, and the commonest kind of urinary gravel are now generally considered to depend on the production in the system of an excess of lithic acid." (*Loc. cit.*) The case from experiments upon which Dr. Garrod was first enabled to draw his reliable conclusions, "was one of chronic gout; and further illustrated the pathology of the disease, by a total absence of lithic acid in the urine, until during the exhibition of colchicum, when its characteristic crystals appeared under the microscope."

Sufficient testimony, it would appear, has been adduced, to render the position tenable which ascribes the gouty paroxysm to an excess of lithic acid, circulating in the blood, and finally deposited in various parts of the body.[1] It does not seem to devolve upon us to describe the phenomena of a fit of the gout—expected as we are, merely to signalize the "effects" of retention of the various elements of the urinary secretion in the blood, we should strictly confine ourselves to such specification, and to the adduction of the best evidence afforded in its support.

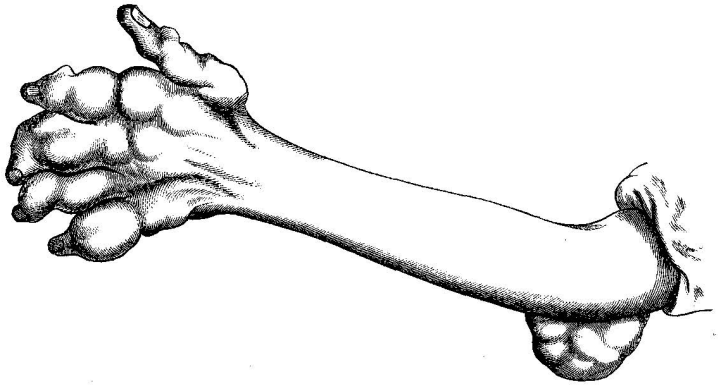
In the first place, then, we may refer the phenomena of gout, more or less completely, to that disorder of the eliminating function of the kidneys, which permits the latter organs to refuse the excretion of uric acid. The latter substance is then necessarily thrown into the circulation, and its tendency—under the circumstances—is to accumulation in the blood. As it accumulates, it is converted, most commonly, into urate of soda, and the deposition of the latter substance upon and into various tissues of the body is a *quasi* vicarious discharge of the uric acid, not excreted by its legitimate channels, the kidneys. This condition is accompanied by the objective phenomena of gout, viz., pain, of an exquisitely acute and torturing character; feverishness, dyspeptic symptoms, and general *malaise*;[2] at the close of the paroxysm, tense, shining, and often excessive swelling of the affected part; finally, entire remission of the symptoms, and better health than before the attack—owing, of course, to the elimination of the *materies morbi*. The *subsequent course* of things will depend very materially upon the habits of the patient, and upon the power he has of restraining his appetites; the fact of hereditary predisposition, or the contrary; and whether the management of the initial attack is judicious, or otherwise. By renewed attacks—chronic gout—the system of course becomes more shattered, less capable of resistance, and less amenable, too often, to remedies. Locally, a variable, often an excessive, amount of injury supervenes. It is at these periods that the lithate of soda—the morbific material—is deposited in various places—principally about the smaller joints. Nature, in her efforts to eliminate this material by other channels than those which are the legitimate ones, does the best she can, but often terribly cripples the subjects of this trying affection (see Fig. 2). Connected with this chronic form of the complaint, we are apt to notice the most troublesome combinations of dyspeptic ailments; and in these the condition of the patient becomes the most unpromising possible, both from the local and from the systemic difficulty. As Dr. Williams states, the uric acid, in such cases, "seems to be engendered in great abundance, and although thrown off in large quantities in the urine for an indefinite period, yet never leaves the body free. Such cases are commonly either hereditary, or those which have been ren-

[1] See Appendix, Note B.

[2] "An impure state of the blood, arising principally from the presence of urate of soda, is the probable cause of the disturbances which not unfrequently precede the seizure, and of many of the anomalous symptoms to which gouty subjects are liable." (A. B. Garrod, *op. cit.*, p. 341.)

dered inveterate by intemperate habits, or neglect of proper treatment." (*Op. cit.*)

Fig. 2.



Elbow and Hand deformed by Gouty Enlargements.—From Dr. Garrod's work (Nature and Treatment of Gout.)

Sequelæ of Gout.—Considering gout as one of the affections ascribable to the retention of uric acid in the blood, let us inquire what are the principal subsequent results. These may, of course, be properly referred to the same cause, as "morbid effects."

We have seen that symptoms of general febrile disturbance, which are of course accompanied by nervous apprehension, fretfulness, heat of skin, more or less sleeplessness, and scanty urine—and which at last is loaded with the lithates, whenever the paroxysm of gout comes on, and at its decline, especially—with hypochondriacism, cramps, flatulence, diarrhœa, but more commonly costiveness (Watson), and more or less general and indescribable *malaise*, both precede and accompany gouty attacks. The dyspeptic symptoms may long remain; although, with care, they may be made sooner or later to disappear.

One of the most serious sequelæ of gout may be considered that wherein the kidneys are affected. Perhaps we may best describe the state we wish to indicate, by terming it the result of a sort of *recoil* upon the kidneys, of the antecedent morbid action in the economy. This is of course entirely the opposite condition of that obtaining when the kidneys fail to eliminate the uric acid, *i. e.*, when their "uric-acid-excreting function" is suspended. In the latter condition of things, we have the blood-disease, the results of which we have sketched above; but when the uric acid begins again to be excreted by its natural passages, the kidneys are very likely to be more or less irritated in the process. There may then be violent pain (*nephralgia*), and nephritis or true inflammation of the substance of the organs may occur. Fully as unfortunate is that state when there is such an amount of uric acid as to be thrown down from the fluid part of the urine—the latter not being sufficient to hold it in solution, and thus carry it out of the body—when it is exceedingly apt to become concreted in various parts of the urinary passages—thus producing obstructions more or less seriously endangering health, and vitiating, in different degrees, the integrity and usefulness of the organs involved. Permanent irritation may thus be maintained; or serious and fatal inflammation be set up; and concretions may be found in

the urinary bladder, which will call for surgical interference for their removal.

Dr. Williams (*op. cit.*), referring to the renal irritation frequently caused in these cases (p. 130, American edition, foot-note), says: "I have in several instances found in the cortical and tubular structure of the kidney, clustered crystals of lithic acid, which, under the microscope, exhibited such sharp angles and dagger-shaped projections, as would afford an easy explanation of the pain, inflammation, and hemorrhage, often attendant on an attack of renal gravel, even when none is obvious in the urine." The same writer reminds us (p. 187), of "the proximity in composition between lithic acid and urea," and that it is probable, according to Liebig, that the former may be converted into the latter. He likewise calls attention to the fact that both gout and rheumatism may give rise to fluxes and catarrhal affections, as oliguria does. Rheumatism and Bright's disease are also, often, nearly related. In respect to this fact, Dr. Garrod announced the following opinions and conclusions, in his paper already quoted (*Med.-Chir. Transactions*, vol. xxxi.), "Blood from patients suffering from Bright's disease and albuminuria after scarlatina, was then examined; the results of these analyses appear to show that—

"1st. Uric acid is always present in the blood in albuminuria. The quantity, however, greatly varies: when the functions of the kidneys are much impaired, it exists in quantities almost as great as in gout; in other cases its amount is small, but it usually exceeds that found in ordinary blood.

"2d. Urea always exists in large quantities in this blood (a fact which has been long since proved), and no relation is found between the amounts of urea and uric acid.

"3d. The kidneys are always deficient in their power of throwing off urea; but with regard to the uric acid, their excreting function may be impaired or not." (*Loc. cit.*)

We thus see what serious disturbances may arise in the system by a perverted condition of secretion, arrest of excretion, and attempts at vicarious elimination of a product which must, in order to the preservation of health, be discharged from the body. The diseases thus produced come clearly under the head of *disordered vital chemistry*. Thus, when the above vital functions are weakened, or totally disabled, there must be not only general disturbance, but, after a time, some special manifestation of disease, and the results of vitiated secretion, decomposition, and over-worked and irritated organs.

The *contracted kidney*—called, by the late Dr. Todd, "the gouty kidney"[1]—and which, as the term he has given it implies, he considered due to the effects, at once irritant, inflammatory, and destructive, arising from gout, we may mention as a result primarily dependent on disorder of the "uric-acid-excreting" function. Dr. Todd has given satisfactory proof (*Clinical Lectures on Certain Diseases of the Urinary Organs*) from cases of patients, of the existence of this form of renal disease. He mentions, also, that many might be inclined to refer it to advanced Bright's disease; but he has signalized it in those who he believes never had that affection. The kidney is shrunken, "and its structure condensed—a condition which, while it may also occur in other states of the system, is

[1] A term objected to by Dr. Barclay (*op. sup. cit.*); who, however, very distinctly recognizes the close connection between gout and renal disease. Valleix, writing in 1853, would not admit that special form of nephritis which is referred to the gouty diathesis.

peculiarly apt to be developed in the inveterate gouty diathesis." (*Loc. cit.*, p. 313.) In one case, necroscopy disclosed hypertrophy of the heart with dilatation—partly due to incrustations on the mitral valve—hardened, condensed, and somewhat contracted liver—the Glissonian capsule being hardened and thickened. The morbid alteration in the latter organ is explained partly by the intemperate habits to which the patient was addicted, "but partly likewise by the share which the liver had in the elimination of the morbid poison of gout." This latter result, which is not infrequent, it is important to notice, as one of the secondary effects of the diverted and retained urinary element. The kidneys in this patient were very much contracted, being hardly one-third of their natural size; they were granular and shrivelled upon their surfaces; the investing capsule was apparently denser and whiter than usual, and was easily detached from the glandular surface. Diminution of the cortical renal substance was the source of the decrease in the size of the organ; two-thirds being estimated to have disappeared. The granulations were noticed likewise upon the cut surface. Dilated and scantily-lined *tubuli uriniferi* were observed on microscopic inspection; from some of them all the epithelial lining had vanished; others were collapsed, folded, and crumpled up; and looked like "fascicles of fibrous tissue." A few fatty epithelial cells were detected in certain *tubuli;* and others of the latter were seemingly healthy, especially those in the pyramids of Malpighi. Dr. George Johnson[1] has described, very minutely, this condition of the kidney, and particularly notes the changes which supervene in the vascular system of the gland. In another instance, Dr. Todd has recorded the discovery, in an inflamed "gouty kidney," of "*opaque streaks of deposit of lithate of soda*" in some of the renal cones. These streaks took the direction of the tubes, and certain of the latter were probably occupied by them.[2] We may well exclaim with Dr. Todd, as we reflect upon these vital manifestations and post-mortem revelations—

"How strikingly do these consequences of the long continuance of the malady comport with the humoral view of the pathology of this disease! Not only are those parts which the morbid matter of gout is most prone to affect, materially damaged, but likewise the emunctories through which the poison would make its escape out of the system—the liver and kidneys: these organs have become poisoned by the morbid matters which have escaped, or tried to make their escape from the system through them; and, therefore, it is natural to expect a considerable change in their nutrition."

It is notorious, however, that in most, if not all, of the *metastases* of gout, there are no traces of morbid action upon the organs affected by the repercussion of the disease. The reason of this doubtless is, that when a fatal result occurs in this manner, the morbid action lasts too short a time, notwithstanding its violence, to leave structural traces. Probably a true *spasmodic* action often destroys the patient, in the thoracic and abdominal varieties of retrocedent gout. It is, however, very likely that in many cases of sudden death from these causes, the vital organs have been previously weakened by disease of some sort; and in many cases chronic gout has inflicted a certain amount of injury, for, as we have already seen, the continued and recurring malady *does* leave its indications, very decidedly, behind it.

[1] On Diseases of the Kidney.

[2] This appearance is also noted by Dr. Garrod, who saw "streaks of white matter at the apex of each pyramid and running up in the direction of the tubuli. Kidneys pale and contracted; cortical portion shrivelled." (p. 199.)

After gout in the *stomach*, Dr. Todd signalizes a "dilated and flaccid state of the organ" as existing, and this is the more marked in proportion as the attacks have been frequent.[1]

In addition to the abundant and often astonishingly copious deposits of the urate of soda into and around the joints, that salt has been found to cover and even to penetrate into the texture of the cartilage investing the affected joints (Watson), and to insinuate itself into the substance of tendons and ligaments (Dr. Wm. Budd). A curious locality is at other times chosen by it—viz., under the skin covering the cartilages of the ears. It has been remarked also over the cartilages of the alæ nasi (Todd).[2] Pus sometimes forms around the variously located depots of urate of soda, and occasionally the discharge of this liquid is quite abundant. Generally speaking, also, the joints of the hands and arms exhibit more plentiful deposits of the urate than those of the lower extremities, except in some forms of acute sthenic gout, when the reverse may be observed. The interference with the motion of the various joints thus affected is so evident and so familiar to practitioners, and indeed so well known to nearly every one, that we hardly need do more than allude to it as a "morbid effect" of the disease. The fact, moreover, has already been made sufficiently prominent.

[1] Op. cit.

[2] Dr. Garrod (op. sup. cit.) states that "sometimes small nodules of urate of soda are found upon the eyelids, especially the lower, now and then in the integuments of the face." He also refers to the great care which is necessary in ascertaining the precise nature of the "white-looking deposits" often occurring about the eyelids and face. Dr. H. Barker saw them on the nose. Dr. Garrod has "observed a true gouty deposit as large as a split pea, apparently attached to the fibrous structure of the corpus cavernosum penis." (p. 86.)

In relation to gouty affections of the eye and ear, Dr. Garrod further remarks: "A form of ophthalmia connected with gout has long been noticed." He adds that it is liable to be confounded with rheumatism, when that is directed to the ocular region. Cases of ophthalmia evidently connected with the gouty diathesis have been observed by Dr. G.; these were instances of conjunctivitis and sclerotitis. "Gouty iritis is also said to occur." The nodules found upon the cartilages of the ear have been mentioned. "Deposits are not unfrequently found upon the drum of the ear, and have been especially pointed out by Mr. Toynbee, but I have failed to discover a trace of uric acid in several examinations of them. Whether they are ever connected with gouty inflammation, is at present a matter of uncertainty; they should especially be sought for in gouty subjects in whom the joints are much affected with chalk-stones, for if not found in such cases, it is not probable that they would occur in others." (pp. 515, 516, op. cit.)

Accomplished aurists have pointedly alluded to the connection between gouty and rheumatic affections and deafness. Mr. William Harvey (The Ear in Health and Disease, London, 1856) specially considers this subject; and we have heard him insist upon the frequency of the connection, whilst observing his aural practice.

In his elaborate work on The Diseases of the Ear, just published (London, 1860), Mr. Toynbee refers to the subject, and furnishes interesting illustrations of the reality of the connection, as observed by himself. He says: "The poison of *gout* may also give rise to deafness and other peculiar symptoms in the head." (See the work cited, page 362, English edition.)

(*To be concluded in next No.*)